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14. ABSTRACT

Objectives: Control of balance requires complex integration of sensory and motor systems. Balance measurement is often over-simplified, preventing balance deficits from being identified and treated after mTBI. Our central hypothesis is that chronic balance deficits after mTBI result from impairments in central sensorimotor integration that may be helped by rehabilitation. This research has two objectives; 1) to characterize balance deficits in people with mTBI, and 2) to use a novel auditory biofeedback device to improve measures central sensorimotor integration and balance control.

Methods: Aim I) Balance Assessment: mTBI patients with non-resolving balance deficits following injury and healthy control participants with no history of mTBI are currently being recruited and tested on a battery of vestibular, neurocognitive, and balance-related tests. Aim II) Balance Rehabilitation: mTBI patients (a subgroup from Aim 1) are randomly allocated into a standard of care balance rehabilitation program either with, or without auditory biofeedback. Both groups receive rehabilitation two times per week for six weeks. All participants are tested at baseline during Aim I testing, and are tested again following the intervention period, and again 6 weeks later to determine retention of changes.

Status: Sixty participants have completed Aim I, Balance Assessment (19 mTBI and 41 controls). Eight of the mTBI participants have fully completed rehabilitation, 6 week post-rehabilitation testing, and the 12 week retention testing (Aim II).

Findings to date: People with chronic mTBI reported worse symptoms relating to balance and vestibular dysfunction than the healthy controls. Vestibular problems associated with the sensation of gravity and linear motion have been noted in the chronic mTBI group. Turning velocity and coordination were slower in people with chronic mTBI. People with chronic mTBI weighted sensory information differently during the test of central sensorimotor integration.

15. SUBJECT TERMS

Balance, mTBI, Rehabilitation, Brain Injury, BESS, Dynamic Posturography, SOT, Inertial Sensors, Auditory Biofeedback, Central Sensory Integration, Concussion

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1. INTRODUCTION:

Control of balance requires complex integration of sensory and motor systems. In the clinic or in the field, balance measurement is often over-simplified, preventing balance deficits from being identified and treated after mTBI. Our central hypothesis is that chronic balance deficits after mTBI result from impairments in central sensorimotor integration that may be helped by rehabilitation. There are two objectives of this proposal; the first objective is to characterize balance deficits in people with mTBI. The second objective is to use a novel auditory biofeedback (ABF) device to improve measures of central sensorimotor integration and balance control.

2. KEYWORDS:

mTBI, Rehabilitation, Brain Injury, BESS, Inertial Sensors, Balance, Auditory Biofeedback, Central Sensory Integration, Concussion

3. ACCOMPLISHMENTS:

What were the major goals and objectives of the project?

Goal	Target Completion Date	Percentage of Completion/ Date of Completion
Specific Aim 1 (Study 1: Assessment n=130 mTBI)		
Major Task 1: Launch Study Activities	*30-Feb-2016*	100%
Major Task 2: Recruitment and Testing (n=130)	*30-Feb-2019*	46%
Major Task 3: Data Analysis and Publications	*30-Sep-2019*	30%
Specific Aim 2 (Study 2: Rehabilitation n=40 mTBI)		
Major Task 1: Launch Study Activities	*30-Feb-2016*	100%
Major Task 2: Prepare Technology and Protocol for Intervention	*30-Sep-2016*	100%
Major Task 3: Randomized Interventions (n=40 mTBI)	*30-Feb-2019*	23%
Major Task 4: Assess Efficacy of Interventions (n=40)	*30-Feb-2019*	15%
Major Task 5: Data Analysis and Publications	*30-Sep-2019*	17%

What was accomplished under these goals?

Status of major activities and specific objectives:

Specific Aim 1 (Study 1: Assessment n=130)

Major task 1: Launch study activities

Subtask 1: Prepare regulatory documents and research protocol

- Prepare FITBIR forms for data reporting; the majority of forms have been published. The CTSIB, Bucket Test, and Symptom Impact Questionnaire are still awaiting publication from FITBIR. The Pain Location Inventory draft has been received by FITBIR and is still pending (awaiting publication status). Data elements for the Short Blessed Test, CSMI, dual-task and instrumented balance tests have all been drafted and sent to FITBIR and we are still waiting to hear back from FITBIR regarding this. The data analyst assigned to our study changed during the submission period. As a result, we have been unable to get updates about the status of these forms. This is a current action item for our team and we are actively following up with the new data analyst at FITBIR to finalize the data elements and create form structures for these study specific tests; 85% complete.

Subtask 2: Prepare technology for study

- Purchasing and testing software of Opals; Validation and reliability testing of the new APDM sensors has been completed; 100% complete *31-JUL-2017.*

Subtask 3: Hiring and training personnel

- All hiring and training of personnel in line with SOW was completed prior to 01-SEP-2016 and documented in the last annual report. The following is an update of hiring and training that was required for replacing staff:
  - Updated research compliance training for new staff; 100% complete 30-*Aug-2017.*
  - Hire and train RA(1) at OHSU; A new RA was hired to replace an RA who left the project in May 2017 100% complete *01-Jul-2017.*
  - Hire and train RA(2) at OHSU; A new RA has been hired to replace an RA who left the project in August 2017. They are currently being trained in procedures; 80% complete.

Major Task 2: Recruitment and testing (n=130)

Subtask 1: Recruitment (n=130)

- Prepare brochures for subject recruitment and meet with primary sources of referral; Updated recruitment fliers to target age ranges 30-60 years old have been approved. We have continued working with Dr. Chesnutt's clinic. We are having research assistants reach out to local clinics and support groups who treat patients with mTBI to post fliers and spread awareness of the study. This will continue to be an ongoing process; 90 % complete.
- Updated recruitment strategy; in the 3rd Quarter report for year 2, we highlighted three objectives to increase recruitment:
  - Placing up recruitment posters on community noticeboards across the city and surrounding neighborhoods.
  - Contact our clinic collaborators on a regular basis to provide a reminder about the study and request their assistance with recruitment.

- Querying the VA databases and EPIC medical charts. Currently we are working with administrators at the VA and OHSU, and the IRB to obtain approval for this method of recruitment.

We are stepping through these strategies currently. This will be an ongoing process; 30% complete.

- Phone screening of subjects; screenings are being performed at OHSU. A telephone recruitment and screening script has been approved by our IRB. This will be an ongoing procedure in the protocol; 38% complete.
- Schedule vestibular/audiogram/ocular motor, CSMI, balance and gait testing; subjects are currently being scheduled for all testing at both locations. This will be an ongoing procedure in the protocol; 37% complete.

Subtask 2: Data collection/management (n=130)

- Schedule testing sites for data collection; subjects are currently being scheduled for their vestibular/audiogram/ocular motor testing, CSMI and balance/gait testing at both OHSU and the VA. This will be an ongoing procedure in the protocol; 49% complete.
- Data collection for the 2 days of data collection for aim 1 takes place; subjects are currently completing their vestibular/audiogram/ocular motor testing, CSMI and balance/gait testing at both OHSU and the VA. This will be an ongoing procedure in the protocol; 46% complete.
- Data back-up onto server including manual data entry; REDCap database setup complete and backup server setup. We have verified both servers and will continue to enter and back up data; 45% complete.
- Screen and verify data on server; check for accuracy; these data check will be performed quarterly. We just completed verification at the end of this quarter and are up to date on data check; 43% complete.
- Upload data to FITBIR; we have submitted data for all published forms, for all subjects tested so far and are in compliance with quarterly reporting requirements. As more forms become published, we will continue to upload data, further, we will continue uploading data quarterly, in accordance with FITBIR guidelines; 35% complete.

Major Task 3: Data analysis and publications

Subtask 1: Data analysis

- Perform all analysis according proposal and share all findings with investigators; we have continued descriptive analysis with data collected to date. Analyses for Study 1 has primarily involved the assessment of turning gait data. This has resulted in a number of presentations and a manuscript submission, described in Subtask 2: Manuscripts and Presentations. Analysis of at home turning data was used as pilot data for a DoD grant application (#DM170579) assessing vestibular dysfunction, submitted during the second quarter. Initial analyses of other data from ANAM neuropsychological testing, vestibular testing, and single-task and dual-task gait testing has begun. Further analysis will be conducted as more data is collected; 30% complete.

Subtask 2: Manuscripts and presentations

- Disseminate findings (abstracts, presentations, papers, DoD), including American Physical Therapy Association and American Congress of Rehabilitative Medicine and rehabilitation journals to share with clinicians;
  - This study has been registered at ClinicalTrials.gov, a site available to the public updated - 100% complete.
  - Preliminary data from the turning gait testing have been presented at:
    - 2017 OHSU Research Week; 100% complete *03-MAY-2017.*
    - The Annual Meeting of the American Society of Biomechanics; 100% complete *11-AUG-2017.*
    - The 2017 Military Health System Research Symposium; 100% complete *27-AUG-2017.*
    - The TBI Symposium: From Research to Recovery on September 16th, 2017; 100% complete *15-SEP-2017.*
  - A paper describing findings from our novel turning task has been submitted to the Journal of Neurotrauma and is currently under peer review; 70% complete.
  - A systematic review paper on single, dual-task and complex gait tasks for use in concussion assessment has been submitted to the journal Gait and Posture and is currently under peer review; 70% complete.
  - A workshop proposal submitted to the 2018 American College of Sports Medicine annual conference has been accepted and will be presented in June 2018; 50% complete.
- Integrate new protocols and head movement metrics into APDM mobility lab system; 0% complete.

Specific Aim 2 (Study 2: Rehabilitation n=40 mTBI)

Major Task 1: Launch study activities

Subtask 1: Hire and train personnel

- All hiring and training of personnel in line with SOW was completed prior to 01-SEP-2016 and documented in the last annual report. The following is an update of hiring and training that was required for replacing staff:
  - Updated research compliance training for new staff; 100% complete 30-*Aug-2017.*
  - Hire and train RA(1) at OHSU; A new RA was hired to replace an RA who left the project in May 2017 100% complete *01-Jul-2017.*

Major Task 2: Prepare technology and protocol for intervention

Subtask 1:

- All tasks completed prior to 01-SEP-2016 and are documented in the last annual review.

Major Task 3: Randomized interventions (n=40 mTBI patients)

Subtask 1:

- PTs call subjects to schedule intervention; subjects are currently being scheduled for the 6-week intervention program; 30% complete.
- 6 week interventions at both sites; for the ease of PT and PT team member, all interventions have been and will continue to take place at OHSU; 23% complete.

- PTs document compliance, adverse events and progression of exercise for each subject; all forms have been created, entered in the database and are currently being used; 23% complete.

Major Task 4: Assess efficacy of interventions (n=40)

Subtask 1:

- Immediate post-test after intervention; nine subjects have completed the intervention and immediate post-test. Preliminary analyses have been conducted using data from these participants. No progress with regards to specifically assessing the efficacy of the intervention has been made over the last quarter; 22% complete.
- Long-term assessment 6 weeks later to assess retention of improvements; No progress with regards to specifically assessing the efficacy of the intervention has been made over the last quarter; 18% complete.

Subtask 2:

- A subset of controls will be tested at a 6 week follow up in order to determine any natural changes in the CSMI test over 6 weeks; eight control subjects have already been assessed and we plan to test 10 subjects; 80% complete.

Major Task 5: Data analysis and publications

Subtask 1: Data Analysis

- Perform all analysis according proposal and share all findings with investigators; preliminary investigation for Study 2 has primarily involved the assessment of CSMI balance data. Initial analyses of turning data has begun, as well as analyses of other data, such as SOT and instrumented balance assessments. Further analysis will be conducted as more data is collected; 17% complete.

Subtask 2: Manuscripts and presentations

- Disseminate findings (abstracts, presentations, papers, DoD), including American Physical Therapy Association and American Congress of Rehabilitative Medicine and rehabilitation journals to share with clinicians;
  - This study has been registered at ClinicalTrials.gov, a site available to the public updated - 100% complete.
  - Preliminary data on sensory weighting and the effects of rehabilitation have been presented at:
    - 2017 OHSU Research Week; 100% complete *03-MAY-2017.*
    - The 2017 Military Health System Research Symposium; 100% complete *27-AUG-2017.*
    - The TBI Symposium: From Research to Recovery on September 16th, 2017; 100% complete *15-SEP-2017.*
  - A protocol paper on the audio biofeedback intervention protocol of this project was accepted and published in BMC Neurology; 100% complete *23-FEB-2017.*
  - An abstract submitted to the APTA Combined Sections Meeting in 2018 has been accepted for verbal presentation and will be presented in February 2018; 70% complete.

Significant Results/ Key outcomes:

We have screened a total of 111 subjects for participation in this study. Of those screened, 62 have been enrolled (20 chronic mTBI and 42 controls). Sixty participants have completed baseline testing (19 chronic mTBI and 41 controls) of the full protocol (Aim 1). Demographic information for these participants is provided in Table 1. Eight of the chronic mTBI participants have fully completed rehabilitation, 6 week post-rehabilitation testing, and the 12 week retention testing (Aim 2). Nine of the control participants have returned to complete the 6 week testing, in order to check the consistency of the measures being assessed (Aim 2). Two chronic mTBI patients have been lost to follow up.

Table 1. Demographics for chronic mTBI and control groups, provided as mean (standard deviation).

	mTBI	**Control**	**P-Value**
Gender (n, %female)	20, 60%	42, 66%	--
Age (years)	40 (11)	33 (11)	0.028
Height (m)	1.72 (0.08)	1.65 (0.27)	0.142
Mass (kg)	80.6 (18.1)	60.5 (28.6)	0.002
BMI	27.0 (4.8)	24.6 (4.3)	0.075
Time since injury (years)	2.9 (3.5)	--	--

People with chronic mTBI reported worse symptoms relating to balance and vestibular dysfunction than the healthy controls. The chronic mTBI group have reported more symptoms and a greater severity of symptoms on the concussion assessment, more symptoms of post-traumatic stress disorder, more symptoms of depression, neurobehavioral symptoms, and have indicated they feel a greater impact caused by these symptoms than the healthy controls (see Table 2).

Table 2. Descriptive statistics from questionnaire data

Test	**mTBI (n=19)**		**Controls (n=41)**		Mean difference	*p*-value
	Mean	SD	Mean	SD		
Short Blessed Test	2.11	2.62	0.95	1.45	1.15	0.086
SCAT-3 # of Symptoms (22)	13.72	6.66	1.29	2.46	12.41	<0.001
SCAT-3 Severity (132)	31.33	18.31	1.41	2.94	29.86	<0.001
PTSD Checklist	44.53	16.40	20.53	6.85	24.00	<0.001
Neurobehavioral Symptom Inventory	34.74	13.67	3.20	3.87	31.54	<0.001
Short Form 36 – General Health	60.79	20.57	80.98	13.14	20.19	<0.001
Pain Location Inventory	5.89	5.40	0.46	0.84	5.43	<0.001
Symptom Impact Questionnaire	44.42	14.98	10.83	8.23	33.59	<0.001
Beck's Depression Inventory	18.17	11.39	2.59	3.22	15.58	<0.001
ANAM Composite Score	-0.51	1.01	0.23	0.90	0.73	0.013

Vestibular problems associated with the sensation of gravity and linear motion have been noted in the chronic mTBI group. Current results indicate differences in vestibular function relating to the otoliths, which sense gravity and linear motion between the chronic mTBI and controls, when the cervical muscle is tested (i.e. cVEMP), but not when ocular muscles are tested (i.e. oVEMP; See Table 3). No key differences emerged

between the mTBI and healthy controls for calorics, a test of the semicircular canals, which sense rotations and orientation in space, and similarly for convergence, a test of eye function and reflex. Similarly, no between-group differences between the chronic mTBI and controls have been noted for the video head impulse test (vHIT), which compares vestibular function in one ear vs. the other.

Table 3. Descriptive statistics for vestibular data

Test		mTBI (n=19)		Controls (n=41)		Mean difference	*p*-value
		Mean	SD	Mean	SD		
Video Head Impulse Test (vHIT)	Right Horizontal Gain	1.01	0.06	0.98	0.09	0.03	0.132
	Left Horizontal Gain	0.92	0.06	0.91	0.12	0.01	0.671
	Symptom Score: Headache	1.13	2.10	0.08	0.36	1.05	0.073
	Symptom Score: Dizziness	1.13	2.20	0.08	0.36	1.05	0.086
	Symptom Score: Nausea	1.13	2.45	0.08	0.49	1.05	0.119
cVEMP	Right Amplitude	105.28	37.55	158.01	82.29	52.73	**<0.001**
	Left Amplitude	91.50	36.23	153.74	84.32	62.23	**<0.001**
	Asymmetry Ratio	42.33	38.31	21.96	28.33	20.37	**<0.001**
	Symptom Score: Headache	1.41	2.21	0.02	0.15	1.39	**0.014**
	Symptom Score: Dizziness	0.65	2.18	0.05	0.31	0.60	0.305
	Symptom Score: Nausea	0.65	2.42	0.00	0.00	0.65	**0.002**
oVEMP	Right Amplitude	10.24	6.11	10.56	6.92	0.32	0.893
	Left Amplitude	11.27	10.02	11.43	8.94	0.17	0.961
	Asymmetry Ratio	22.57	28.63	20.90	22.30	1.67	0.846
	Symptom Score: Headache	1.65	1.77	0.29	0.72	1.35	**0.007**
	Symptom Score: Dizziness	0.59	1.06	0.07	0.47	0.52	0.070
	Symptom Score: Nausea	0.29	0.59	0.10	0.62	0.20	0.264
Convergence	Trial 1	8.82	11.18	3.79	4.33	5.04	0.088
	Trial 2	7.59	10.22	4.70	4.78	2.89	0.278
	Trial 3	8.32	11.72	4.55	4.70	3.77	0.215
	Symptom Score: Headache	0.83	1.58	0.07	0.26	0.76	0.058
	Symptom Score: Dizziness	0.33	0.84	0.00	0.00	0.33	0.111
	Symptom Score: Nausea	1.00	1.46	0.00	0.00	1.00	**0.010**
Calorics	Right Warm SPV	22.71	13.29	24.75	18.18	2.04	0.659
	Left Warm SPV	19.43	8.89	20.87	14.15	1.44	0.665
	Right Cold SPV	16.67	9.97	22.13	14.44	5.46	0.121
	Left Cold SPV	18.64	12.00	18.58	10.45	0.07	0.985
	Unilateral Weakness	16.23	14.08	19.79	13.60	3.56	0.435
	Symptom Score: Headache	2.64	2.37	0.38	1.48	2.27	**0.004**
	Symptom Score: Dizziness	3.15	2.79	1.13	1.98	2.03	**0.025**
	Symptom Score: Nausea	1.71	2.43	0.40	1.22	1.31	0.071

Turning velocity and coordination were slower in people with chronic mTBI. A novel turning task has been used to evaluate turning gait. The chronic mTBI group were unable to complete the turning course at the same speed as the healthy controls, as indicated by slower average lap times (mTBI mean, SD = 20.3, 7.1 s; Control mean, SD = 16.5, 1.9 s; t = 2.74 p = 0.009). The analysis of turning data revealed that the chronic mTBI group turned their upper body and lower body slower than the controls when turning (see Table 4).

Table 1. Univariate descriptive means (standard deviations) for segmental coordination timing (ms) by each turning angle measured.

	mTBI	Control
45 Degree Angle	203.0 (199.4)	128.3 (109.5)
90 Degree Angle	161.1 (117.0)	80.4 (76.5)
135 Degree Angle	97.3 (158.3)	74.2 (84.9)

The chronic mTBI group also exhibited a longer delay between the peak rotation speed of the head and the peak rotation speed of the lower body (β=0.096, SE=0.039, p=0.015). Additionally, this delay was more variable in the chronic mTBI group (β=0.095, SE=0.027, p=0.001).

People with chronic mTBI weighted sensory information differently during the test of central sensorimotor integration. When reliance on the vestibular and visual systems was tested using the central sensorimotor integration test (CSMI), the chronic mTBI exhibited lower weight scores (W), indicating that they weighted sensory information from the vestibular and visual systems lower than the healthy controls. The chronic mTBI group also had lower stiffness and damping values. Lower stiffness and damping in the chronic mTBI group suggests a lesser ability to control their body sway.

Table 5. Descriptive means (standard deviations) for the performance on CSMI test evaluating reliance on vestibular and visual systems for chronic mTBI and control groups. Cohen's *d* represents the difference between groups.

	mTBI	Control	*d*	Interpretation
W	0.63 (0.06)	0.71 (0.06)	-1.43	Large effect
Kp	1.57 (0.22)	1.73 (0.36)	-0.57	Medium effect
Kd	0.47 (0.06)	0.57 (0.10)	-1.17	Large effect

Following rehabilitation, the mTBI group increased their sensory weight score, suggesting that they placed a greater reliance on the vestibular and visual systems, and relied less upon inaccurate proprioceptive information. In addition, the mTBI group had increased stiffness and damping values following rehabilitation, suggesting an improved control of their body sway.

Table 6. Descriptive means (standard deviations) for the performance on CSMI test evaluating reliance on vestibular and visual systems before and after rehabilitation. Cohen's *d* represents the difference between baseline and post-rehabilitation values.

	Baseline	Post-rehabilitation	*d*	Interpretation
W	0.63 (0.06)	0.69 (0.04)	1.20	Large effect
Kp	1.57 (0.22)	1.61 (0.10)	0.26	Small effect
Kd	0.47 (0.06)	0.53 (0.03)	1.22	Large effect

What opportunities for training and professional development has the project provided?

The research team has had the opportunity to attend a number of conferences and meetings in order to meet with experts in the field of research. Two of the key meetings include the Military Health System Research Symposium (MHSRS) and the TBI Symposium: From Research to Recovery, discussed below.

Three members of the project team, Dr. Laurie King (PI), Dr. Lucy Parrington (post-doctoral fellow), and Dr. Peter Fino (post-doctoral fellow) each attended the MHSRS in Kissimmee, Florida, August 2017. Dr. Fino and Dr. Parrington presented preliminary findings from the current study. The conference provided the opportunity for these research team members to discuss current and future work, as well as further develop networks and collaborations with other mTBI researchers. While in attendance at the MHSRS, Dr. King, Dr. Parrington, and Dr. Fino also attended a meeting with researchers from across the country working in the area of mTBI to discuss return to duty decisions for military members.

Dr. Parrington and Dr. Fino presented at the 2017 annual TBI Symposium: From Research to Recovery on September 15th and 16th, 2017. A number of experts involved in mTBI research from California, Oregon and Washington were in attendance. Prior to presenting, Dr. King, Dr. Parrington and Dr. Fino were invited to a lunch to discuss collaborations with other researchers.

How were the results disseminated to communities of interest?

This work has resulted in the following journal publications:

- Fino PC, Peterka RJ, Hullar T, Murchison C, Horak FB, Chesnutt JC, King LA. (2017). Assessment and rehabilitation of central sensory impairments for balance in mTBI using auditory biofeedback: a randomized clinical trial. *BMC Neurology*, 17:1, 41-55.
- Fino PC, Parrington L, Walls M, Sippel E, Hullar TE, Chesnutt JC, & King LA. (Under Review). Abnormal turning and its association to self-reported symptoms in chronic mTBI.

Research findings have been disseminated locally and nationally through conference presentations including:

- Fino PC, Parrington L, Walls M, Sippel E, King LA. (2017). Slower turning velocity and increased coordination variability are associated with self-reported symptoms in adults with mTBI. *Military Health System Research Symposium*. Kissimmee, FL, August 27-30. Oral

- Parrington L, Fino PC, Peterka R, Chesnutt J, Walls M, Sippel E, Wilhelm J, Schlimgen J, King LA. (2017). The effects of rehabilitation on sensory reweighting in patients with chronic mTBI. *Military Health System Research Symposium*. Kissimmee, FL, August 27-30. Oral
- Fino PC, Parrington L, Walls M, Sippel E, King LA. (2017). Segmental turning velocity and coordination in adults with mTBI. *41st Annual Meeting of the American Society of Biomechanics*. Boulder, CO, August 8-11. Thematic Poster

Research findings have been disseminated through the following oral presentations:

- Parrington, L (2017). The effects of rehabilitation on sensory reweighing in patients with chronic mTBI. *TBI Symposium: From Research to Recovery, Oregon Health and Science University. September 15.* Oral
- Fino, PC (2017). Abnormal Turning and its Association with Symptoms in Chronic mTBI. *TBI Symposium: From Research to Recovery, Oregon Health and Science University. September 15.* Oral

What do you plan to do during the next reporting period to accomplish the goals?

The strategies for recruitment implemented during the period July-September 2017, have been successful in increasing the number of participants recruited and enrolled. Now that we have an RA promoting awareness of the study at OHSU and affiliated clinics, we hope to increase the number of chronic mTBI patients recruited and enrolled. In addition to that, we are working through other steps identified under the updated recruitment strategy, Major Task 2, Subtask 1: Recruitment. We believe that working through this plan should help us reach our recruitment targets.

We also plan to continue data analysis during the next reporting period, focusing on other areas of analysis, such as the vestibular data, the ANAM neurocognitive testing, and the straight light single-task and dual-task gait data. We have begun assessments on each of these, and will continue to progress the analyses over the next reporting period.

4. IMPACT:

What was the impact on the development of the principal discipline(s) of the project?

This project is allowing researchers in the area of mTBI to understand more about the role that sensory integration plays in chronic balance deficits. Furthermore, it is creating awareness in clinicians of the need to use more objective measurements of balance deficit. As we progress through the study, we hope that this project will give insight into how audio biofeedback can be used to help the rehabilitation process, by helping to guide and recalibrate the way people use (i.e. integrate) their sensory information to balance and perform day to day tasks. We believe this research will impact clinical practice, by first, providing information on how to more objectively quantify chronic balance problems related to mTBI, and second, in guiding the standard of care to use audio biofeedback technology.

What was the impact on other disciplines?

Our research team meets once per month with OHSU doctors, physical therapists and athletic trainers, as well as clinicians from other affiliated clinics who treat patients who have sustained an mTBI. At these meetings, we are able to discuss research findings, and further, how we can translate this knowledge into clinical practice. We are also able to gain insight from clinicians about current policy and practice. In addition to this, members of

our team participated in the 2017 TBI Symposium: From Research to Recovery, which involved research sessions on day one and clinical sessions on day two. The TBI Symposium had visitors from California (Stanford University) and across the Pacific Northwest including Eugene (University of Oregon) and Seattle (University of Washington), and provided opportunity for researchers and clinicians to engage in discussion about chronic balance problems in TBIs.

What was the impact on technology transfer?

Information about the central sensorimotor integration (CSMI) test and sensory weighting were presented at the Military Health System Research Symposium (MHSRS), August 27, 2017. Following this presentation, a number of researchers indicated their interest in using this test. As a result of discussions at the MHSRS, we have begun work on a methods-based manuscript, which will provide details on how the NeuroCom Clinical Research System™ can be customized for the CSMI protocol. This paper will help transfer knowledge to other researchers in the field, and promote the use of this method for analyzing balance dysfunction in persons with chronic balance problems following mTBI and other balance impaired populations.

What was the impact on society beyond science and technology?

In March 2017 members of our team attended the OHSU Brain Fair, an annual event held at the Oregon Museum of Science and Industry (OMSI). The fair is open to the public and is attended by people of all ages. Our research team were in attendance at a booth, and were able to perform demonstrations and explain how wearable sensors can be used to provide objective measures of balance, and the importance of this type of testing in people with chronic balance problems following mTBI.

Our research team also works mentoring high-school students by providing them with the opportunity to learn about our study, and complete independent mini projects to help build their knowledge in the area of mTBI, balance and gait.

5. CHANGES/PROBLEMS:

Changes in approach and reasons for change

Nothing to Report

Actual or anticipated problems or delays and actions or plans to resolve them

There have been no problems or delays to report for the last quarter that have not been resolved. During August a second research assistant (RA) left the project. The RA who left in August was a different RA to the one we had previously reported as leaving. This had little impact on our timeline in comparison to the delays indicated previously when a RA left in May (Year 2, Quarter 2 report). Despite that this was an unanticipated change in staff, we were much better prepared and have been able to make a smoother transition including hiring and training a new RA within a short timeline. The new hire has made great progress throughout September in learning the testing protocol and other requirements associated with the project. We do not believe that this has caused any major delays.

One reportable new event occurred in this Quarter, in which members of the study team were missing regulatory documents within the IRB. This event was reported to the IRB (and DoD) and reviewed. The IRB determined that this event was not serious and this has now been resolved. A copy of the review of reportable event letter is provided in the Appendix.

All other reporting of problems and delays have been described in previous quarterly reports. These problems and delays have been provided again below, verbatim, for consistency with previous reports.

Actual or anticipated problems identified in Year 2 Quarter 2 report (taken from prior report):

1) We have come across some minor issues with home-monitoring data, where some patients have failed to wear the sensor for a long enough period of time, or have forgotten to wear the sensor for a day. This has meant that some participants have a limited sampling of their mobility data in comparison with others. This is seen as a minor problem, however, to mitigate this issue in the future, we will incorporate a contacting of participants throughout the home monitoring period to remind them to put their home sensor on to track their movements.
2) The primary anticipated problem surrounds the change of research assistants (RAs) that will take place during May. Unfortunately, we will lose one of our highly skilled RA's in the next quarter. The role of the current research assistant is multifaceted and requires a diverse skillset. The role requires knowledge about the upkeep of secure databases, data management, and subject recruitment, testing procedures and running the rehabilitation sessions for the intervention. Even with a highly capable new RA, the training and upskilling required will be time consuming for the current RAs and may reduce their current capacity, making this a major hurdle for the next reporting period.
3) In order to help mitigate circumstances, we have begun looking at suitable candidates for the position so that the new RA can interview early in the next quarter and can begin each of the learning modules required to work on this project. We will also ensure that a new IRB request for adding the new hire on the project as soon as they have been selected for the position. Once they have been cleared by the IRB to work on the project, they will begin shadowing the current RAs in order to learn as much as possible without impeding progress.
4) Another anticipated problem, as with our last quarterly report is the ongoing challenge of recruitment of mTBI patients. We have recently updated the flyer for this project (cleared through the IRB) and hope that this will help with our recruitment process. Recruiting participants has been indicated as a top priority and we have discussed a number of strategies to improve recruitment, which we will look to implement in the next quarter. Having successfully enrolled a number of participants in the rehabilitation program during this reporting period, we hope to see slight increase in the level of recruitment and participation throughout the next quarter.

Actual or anticipated problems identified in Year 2 Quarter 3 report:

- During two separate testing sessions we have had delicate pieces of equipment which have broken during testing and have been required to be fixed before testing to proceed. On one occasion this required the participant to be re-booked in for testing. This participant was unable to return during an appropriate time period for testing and was therefore considered as lost to follow up. For this participant, all measures were able to be collected on tests that were unaffected by the equipment issue. To

circumvent this issue in the future, we have organized for replacement parts, which can be switched if broken, to remain in the testing room.

- One of the key anticipated problems identified in the last quarterly report involved the changeover of research assistants (RA's) on the project. The primary focus of this quarter has involved the training of a new RA to run the rehabilitation program and the full testing protocol. We have successfully trained up a new RA who is now fully competent in the required areas. As a result of this focus shift to train the RA, we have been unable to place as much focus on the recruitment and enrollment of patients this quarter. In addition to this, with no longer having an RA affiliated with the Veterans Affairs (VA) Portland Health Care System, our OHSU RA's have been required undertake time consuming processes to gain access to the VA databases for recruitment purposes.
- We are currently ahead of target for our recruitment of participants from OHSU and the wider community. The combination of changing RA's and losing an RA at the VA, however, has resulted in a delay in the recruitment of participants from the VA. As a team, we are aware of this delay and have discussed a range of strategies to increase the number of recruited and enrolled participants. Part of this strategy involves querying the VA databases to retrieve a list of patients to contact regarding research. Each potential volunteer will then be sent a letter in the mail to confirm if they are happy to be contacted regarding the study.

Changes that had a significant impact on expenditures

Nothing to report

Significant changes in use or care of human subjects, vertebrate animals, biohazards, and/or select agents

Nothing to report

6. PRODUCTS:

Publications, conference papers, and presentations

Publications, conference papers, and presentations submitted, accepted, and presented during the reporting period October 2016 to September 2017:

Manuscript accepted in BMC Neurology

- Fino PC, Peterka RJ, Hullar T, Murchison C, Horak FB, Chesnutt JC, King LA. (2017). Assessment and rehabilitation of central sensory impairments for balance in mTBI using auditory biofeedback: a randomized clinical trial. BMC Neurology, 17:1, 41-55.

Manuscript submitted to the Journal of Neurotrauma

- Peter C Fino, Lucy Parrington, Merissa Walls, Emily Sippel, Timothy E Hullar, Laurie A King; Abnormal turning and its association to self-reported symptoms in chronic mTBI; submitted and under review.

Manuscript submitted to the Gait & Posture

- Peter C. Fino, Lucy Parrington, Will Pitt, Douglas N. Martini, James C. Chesnutt, Li-Shan Chou, Laurie A. King; Detecting Gait Abnormalities After Concussion or Mild Traumatic Brain Injury: A Systematic Review of Single-Task, Dual-Task, and Complex Gait; submitted and under review.

Conference abstracts presented at OHSU Research Week (Oregon Health & Science University, May 1-3, 2017) – poster presentations

- Lucy Parrington, Peter C Fino, Robert Peterka, James Chestnutt, Merissa Walls, Emily Sippel, Jenny Wilhelm, Jeff Schlimgen, Laurie A King; The effects of rehabilitation on sensory reweighting in patients with chronic mTBI.
- Peter C Fino, Lucy Parrington, Merissa Walls, Emily Sippel, Laurie A King; Slower turning velocity and increased coordination variability are associated with self-reported symptoms in adults with mTBI.

Conference abstract presented at the American Society of Biomechanics conference (University of Colorado, Boulder, August 8-11, 2017) – poster presentation

- Peter C Fino, Lucy Parrington, Merissa Walls, Emily Sippel, Laurie A King; Segmental turning velocity and coordination in adults with mTBI; ASB40.

Conference abstracts presented at the Military Health System Research Symposium (Kissimmee, FL, August 26-30, 2017) – oral presentations

- Lucy Parrington, Peter C Fino, Robert Peterka, James Chestnutt, Merissa Walls, Emily Sippel, Jenny Wilhelm, Jeff Schlimgen, Laurie A King; The effects of rehabilitation on sensory reweighting in patients with chronic mTBI.
- Peter C Fino, Lucy Parrington, Merissa Walls, Emily Sippel, Laurie A King; Slower turning velocity and increased coordination variability are associated with self-reported symptoms in adults with mTBI.

Conference abstract accepted for presentation at the Combined Sections Meeting, February 21-24, 2018, New Orleans, LA – oral presentation

- Lucy Parrington, Peter C Fino, Robert Peterka, James Chestnutt, Merissa Walls, Emily Sippel, Jenny Wilhelm, Jeff Schlimgen, Laurie A King; Rehabilitation and sensory reweighting in patients with chronic mTBI.

Workshop proposal accepted for presentation at the American College of Sports Medicine Annual Meeting (The 9th World Congress on Exercise is Medicine), May 29-June 2, 2018, Minneapolis, MN

- Laurie A King; Lucy Parrington; Wearable sensors and the instrumented assessment of balance and gait after concussion.

Presentations given at the TBI Symposium: From Research to Recovery, Oregon Health and Science University. September 15, 2017 – oral presentations

- Lucy Parrington: The effects of rehabilitation on sensory reweighting in patients with chronic mTBI.
- Peter Fino: Abnormal Turning and its Association with Symptoms in Chronic mTBI.

Website(s) or other Internet site(s)

Dissemination of research through internet and social media during the reporting period October 2016 to September 2017

- Blog post on the OHSU Brain Institute site providing a lay explanation of preliminary findings from the study:

  Lucy Parrington; OHSU research targets chronic balance dysfunction in mTBI patients. OHSU Brain Institute blog post <http://www.ohsu.edu/blogs/brain/2017/09/21/ohsu-research-targets-chronic-balance-dysfunction-in-mtbi-patients/>

- OHSU Brain Institute (@OHSUBrain) Twitter feed and link to OHSU Brain Institute blog post indicated above.

  OHSU Brain Institute Twitter feed
  <https://twitter.com/OHSUBrain/status/911252002100977664>

Technologies or techniques

Nothing to report

Inventions, patent applications, and/or licenses

Nothing to report

Other products

Preliminary findings from this study were used as pilot data for a DoD grant application titled Monitoring effects of vestibular dysfunction on balance and head-trunk coordination in clinical and operational environments (#DM170579) submitted during the reporting period October 2016 to September 2017.

PARTICIPANTS & OTHER COLLABORATING ORGANIZATIONS:

What individuals have worked on the project?

Name:	Nicholas Kreter
Project Role:	*Research Assistant 1*
Researcher Identifier (e.g. ORCID ID):	*N/A*
Nearest person month worked:	1
Contribution to Project:	*Mr. Kreter has performed data collection and data entry.*
Name:	*Laurie King* - No Change
Name:	*Lucy Parrington* - No Change
Name:	*Alexa Beeson* - No Change
Name:	*Robert Peterka* - No Change
Name:	*Peter Fino* - No Change
Name:	*Sean Kampel* - No Change
Name:	*Marco Juardo* - No Change

Has there been a change in the active other support of the PD/PI(s) or senior/key personnel since the last reporting period?

Yes, Dr. King had a change in her other support. 1 R21 HD080398 02 ended on 7/31/17. Due to this, her effort on MR141257 has increased from 4 calendar months to 8 calendar months.

What other organizations were involved as partners?

Nothing to report

7. SPECIAL REPORTING REQUIREMENTS:

None

8. APPENDICES:

Copy of reportable event letter

REVIEW OF REPORTABLE EVENT

October 4, 2017

Laurie King

Dear Laurie King:

On 9/26/2017 7:00 AM, the IRB reviewed the following new information report:

- Study team members missing Scope of Work (SOW) and Research Personnel Change Form (RPCF)

This information is regarding:

Title:	PVAMC/OHSU J: Rehabilitation of Central Sensory Impairments for Balance in mTBI
Principal Investigator:	Laurie King
RNI ID:	RNI00001458
IRB ID:	STUDY00015010

This IRB determined that this event is noncompliance that is not serious or continuing.

The IRB determined that this event is also a Research Information Security Incident; the incident does not constitute a serious problem.

Actions Required:
The study team has confirmed that Merissa Walls and Emily Sippel no longer work in the Laboratory, so no action will be needed for these people. However, the study team has stated they will add the SOW and RPCF form for the other team members (Dr. Peterka and Dr. Fino) so that they will be in compliance if they need to help work on the VA side of the study in the future. Going forward, the study team will ensure that each new team member who may need to help test on the VA side of the study will have not only their WOC completed but also the 2 additional forms (SOW and RPCF) that we were missing for this incident.

Version Date: 06.29.17 Page 1 of 2

OHSU Research Integrity Office
3181 SW Sam Jackson Park Road - L106RI
Portland, OR 97239-3098
(503)494-7887 irb@ohsu.edu

VA Research and Development Service
3710 SW U.S. Veterans Hospital Road - R&D
Portland, OR 97239-2999
(503)273-5152 pvamc-irb@va.gov

The study team's proposed remedial actions are sufficient and no actions beyond those are needed.

Sincerely,

The OHSU IRB office

Conference abstracts

Presented at Oregon Health & Science University 2017 Research Week

The effects of rehabilitation on sensory reweighting in patients with chronic mTBI

Lucy Parrington[1], Peter Fino[1,6], Robert Peterka[2,3,] James Chesnutt[4], Merissa Walls[1,6], Emily Sippel[1,6], Jenny Wilhelm[5], Jeff Schlimgen[5], Laurie King[1,6]

1) Department of Neurology, Balance Disorders Laboratory, Oregon Health & Science University, Portland, USA
2) National Center for Rehabilitative Auditory Research, VA Portland Health Care System
3) Department of Biomedical Engineering, Oregon Health & Science University, Portland, USA
4) Orthopaedics and Rehabilitation, Oregon Health & Science University, Portland, USA
5) Department of Rehabilitation Services, Oregon Health & Science University, Portland, USA
6) VA Portland Health Care System, Portland, USA

Keywords: mTBI, balance, sensorimotor integration, rehabilitation

This abstract presents preliminary findings assessing the effects of targeted rehabilitation on sensory weighting in patients with chronic balance impairment following mTBI. Patients with chronic imbalance complaints after mTBI (*n*=4) and controls with no recent history of mTBI (*n*=7) were recruited through Oregon Health & Science University and VA Portland Health Care System. Sensory weight scores were measured using a novel test of central sensorimotor integration. This procedure provides an indication through weight scores, which allow the evaluation of reliance on proprioceptive, vestibular or visual systems. Following baseline testing, patients were enrolled into a rehabilitation program (2x/week for 6 weeks) focused on maintaining balance under changing sensory conditions with increasing levels of difficulty. Follow-up testing was conducted at the conclusion of the intervention for people with mTBI and six weeks after baseline testing in controls, to establish stability of the measure. Changes in sensory weight scores were assessed using Cohen's *d* effect sizes. Large effects in the first two conditions tested suggest changes in vestibular and combined vestibular/visual weight in the rehabilitation group (*d*=0.86, *d*=1.87, respectively) but not in controls (*d*=0.08, *d*=0.09, respectively). Small and medium effects were found following rehabilitation for combined proprioception/vestibular systems (*d*=0.43) and vestibular system with conflicting visual/proprioceptive information (*d*=0.69), while only small effects were noted in the controls (*d*=0.30, *d*=0.42, respectively). Results suggest that people with chronic mTBI may be able to change the level of reliance on proprioceptive, vestibular or visual systems, which has practical applications for rehabilitation in patients suffering ongoing balance impairment.

Slower turning velocity and increased coordination variability are associated with self-reported symptoms in adults with mTBI

[1,2] Peter C. Fino, [1] Lucy Parrington, [1,2] Merissa Walls, [1,2] Emily Sippel, and [1,2] Laurie A. King

[1] Oregon Health & Science University, Portland, OR, USA
[2] Veterans Affairs Portland Health Care System, Portland, OR, USA

In daily activity, turning is common and requires rapid, coordinated reorientation of the head and trunk towards the new direction of travel. Yet, turning gait has not been well explored in populations with mTBI. We hypothesized that individuals with mTBI would reduce their reorientation velocity and increase the variability of head-to-trunk coordination compared to controls, and that reduced velocity and increased variability would be associated with their self-reported symptom score. Ten adults with mTBI and 25 controls provided informed consent. All mTBI participants had complaints of imbalance and a diagnosed mTBI for >3 months. Participants completed the Neurobehavioral Symptom Inventory (NSI) before walking 12 self-paced laps around a course containing various turns. Inertial sensors over the forehead and lumbar region collected angular velocities of the head and trunk, respectively. Linear mixed models compared the peak angular velocities of each turn between groups after adjusting for covariates of turning angle and walking speed. Independent sample t-tests compared coordination variability between groups. Pearson correlation coefficients compared the relationship between each outcome and NSI symptom scores in the mTBI group. After adjusting for walking speed and turning angle, participants with mTBI had slower peak angular velocities of the head (p=0.01) and trunk (p<0.01) compared to the control group. Head-trunk coordination variability was higher in mTBI participants (p<0.01). Slower head velocity and increased coordination variability were strongly associated with NSI symptom scores (p<0.01, p<0.01). The association of turning outcomes to symptoms suggests individuals with mTBI change reorientation patterns to minimize the exacerbation of symptoms.

Presented at the 2017 Annual Meeting of the American Society of Biomechanics, Boulder, CO

SEGMENTAL TURNING VELOCITY AND COORDINATION IN ADULTS WITH MTBI

[1,2] Peter C. Fino, [1] Lucy Parrington, [1,2] Merissa Walls, [1,2] Emily Sippel, and [1,2] Laurie A. King

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INTRODUCTION

Abnormal standing balance and straight gait have been widely documented in individuals following mild traumatic brain injury (mTBI) [1]. Yet, daily activities require complex movements that involve change of direction and coordinated head and trunk reorientation [2]. Sport-related concussion has been associated with increased intersegmental coordination variability during unplanned turns [2] and decreased center-of-mass speed and curvature when walking around an obstacle [3], but planned turning tasks have not been well explored in populations with mTBI. In particular, it is unclear whether turning performance is associated with self-reported symptoms in individuals with mTBI. As rapid head movements can exacerbate symptoms, individuals reporting mTBI symptoms may limit the velocity of reorientation based on their symptoms. We hypothesized that individuals with mTBI would reduce their reorientation velocity and increase the variability of head-to-trunk coordination during planned turns compared with controls. Further, we hypothesized that the reduction in the velocity and increase in variability would be associated with their self-reported symptom score.

METHODS

Ten individuals with mTBI {mean (SD) age = 34 (6.7) years, height = 171.8 (8.4) cm, mass = 90.7 (19.9) kg} and 25 healthy controls {age = 28 (8.4) years, height = 169.3 (8.46) cm, mass = 70.3 (13.9) kg} provided informed written consent to participate. All mTBI participants had self-reported complaints of imbalance and a diagnosed mTBI >3 months before the testing session. At the beginning of each session, participants completed the Neurobehavioral Symptom Inventory (NSI). Participants then walked at their comfortable pace around a marked course containing four 45° turns, four 90° turns, and two 135° turns (Figure 1). Each participant completed 12 continuous laps of the course. The first and last laps were excluded from the analysis. Walking speed was determined from the average time to complete each lap. Inertial sensors affixed over the forehead and lumbar region of the spine collected angular velocities of the head and trunk, respectively.

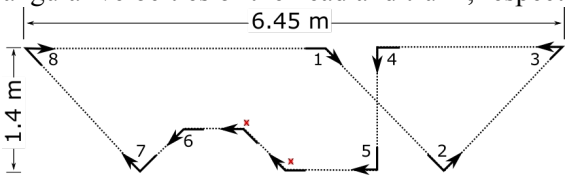

Figure 1: Turning course marked with arrows. Eight turns were analyzed, 2 turns (red x) were excluded.

Angular velocities were low-pass filtered at 1.5 Hz. For each turn, the magnitude and time of each peak axial angular velocity was extracted for the head and trunk. Two 45° turns were excluded from the analysis because a clearly defined peak velocity was lacking across all participants. Head-to-trunk coordination was defined as the lag time, calculated as the difference in time between peak velocities of head and trunk for each turn (Figure 2).

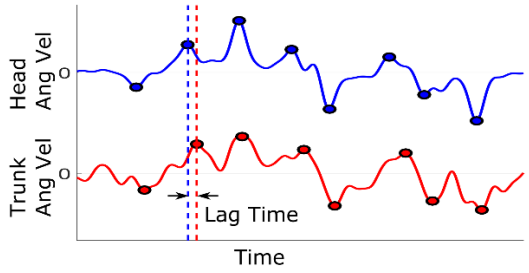

Figure 2: Example angular velocity traces showing the peak for each turn (markers) and lag time.

For each participant, the peak angular velocities were averaged across turns of the same angle. Lag time and lag time variability were determined from the mean and standard deviation, respectively, across all turns. Linear mixed models compared the average peak angular velocities between groups after adjusting for covariates of age, height, mass, walking speed, and turning angle. Independent sample t-tests compared lag time and lag time variability between groups. Pearson correlation coefficients compared the relationship between each

outcome and NSI symptom scores within the mTBI group.

RESULTS AND DISCUSSION

After adjusting for covariates of age, height, weight, walking speed, and turning angle, participants with mTBI had significantly slower peak angular velocities of the head (Figure 3, $p < 0.01$, $\beta = -0.30$, SE = 0.11) and trunk ($p < 0.01$ $\beta = -0.31$, SE = 0.11) compared with the control group. Lag time did not differ between groups, but lag time variability was significantly higher in the mTBI group compared with the control group ($p < 0.01$, $g = 0.58$).

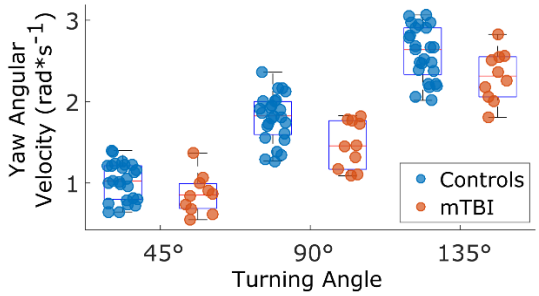

Figure 3: Average peak yaw angular velocity of the head for each participant for each turn angle.

Within the mTBI group, NSI total symptom scores were associated with slower average peak angular velocities of the head and trunk during 90° turns ($r = -0.77$, $p < 0.01$; $r = -0.71$, $p = 0.02$). Lag time variability was strongly associated with NSI symptom scores (Figure 4, $r = 0.87$, $p < 0.01$).

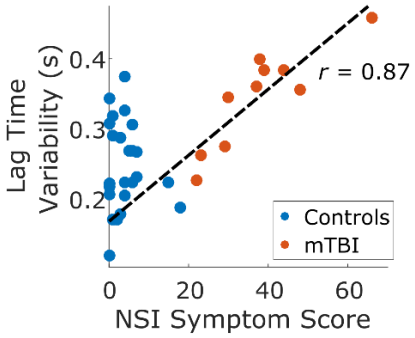

Figure 4: Lag time variability was associated with NSI total symptom score in the mTBI group.

The slower peak velocities found in the mTBI group are consistent with previous reports of slower center-of-mass velocities in asymptomatic concussed athletes during a 90° turn [3]. Notably, the slower angular velocities were significant after adjusting for walking speed, suggesting that the mTBI group may have cut corners to reduce the curvature [3] and angular velocity of each turn. Additionally, our results extend the evidence of increased segmental variability, previously reported during a light-induced turning task [2], to preplanned turns.

Importantly, measures of turning were associated with symptom scores. Standing balance and straight gait deficits are common after mTBI, but they have not been associated with symptom scores [4]. The association between higher symptom scores and measures of turning may be indicative of active avoidance of rapid rotations to prevent exacerbating symptoms. Alternatively, it could suggest symptoms are more apparent during specific dynamic activities such as turning, and such activities may heavily influence the self-reported symptom score given the high prevalence of turning in everyday locomotion. Further study of turning in symptomatic and asymptomatic individuals with mTBI is warranted.

CONCLUSIONS

Individuals with mTBI adopted slower turning velocities across all turning angles, and exhibited more variable head-to-trunk coordination compared with controls. These results provide knowledge of how self-reported symptoms influence daily locomotor function in adults with mTBI. The association of turning velocity and head-to-trunk coordination variability to self-reported symptoms suggests individuals with mTBI change reorientation patterns to minimize the exacerbation of symptoms.

REFERENCES

Guskiewicz KM, *Clin Sports Med,* 30.1, 89-102, 2011
Powers KC, et al. *Gait Posture*, 39.2, 728-32, 2014.
Fino PC, et al. *J Neuroeng Rehabil*, 13.65, 1-15.
Guskiewicz KM, et al. *J Athl Train,* 36.3, 263-73, 2001

ACKNOWLEDGMENTS

Funding was provided by the US Department of Defense (W81XWH-15-1-0620)

Presented at the 2017 MHSRS meeting in Kissimmee, FL

The effects of rehabilitation on sensory reweighting in patients with chronic mTBI

Lucy Parrington[1], Peter Fino[1,6], Robert Peterka[2,3,] James Chesnutt[4], Merissa Walls[1,6], Emily Sippel[1,6], Jenny Wilhelm[5], Jeff Schlimgen[5], Laurie King[1,6]

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7)

Background: Balance impairments are a common complaint in patients suffering chronic effects of mild traumatic brain injury (mTBI) (Vanderploeg et al., 2007). Further, recent research has indicated vestibular and visual integration dysfunction is linked to postural instability in military service members with mTBI (Haran, et al., 2016). We propose that central sensorimotor integration disorders underlie chronic balance impairments and thus quantitative assessment of sensorimotor integration would have practical clinical applications for characterizing balance deficits and tracking recovery in Warfighters. This abstract presents preliminary findings from a larger study assessing the effects of targeted rehabilitation on sensory contributions to balance (sensory weights) under various test conditions using a novel test of central sensorimotor integration (CSMI) (Peterka, 2002).

Methods: Patients (*n*=4, age=33.3±8.65) and controls (*n*=7, age=25.9±6.08) were recruited through Oregon Health & Science University and VA Portland Health Care System. Participants were between 21-50, had either chronic complaints of imbalance after mTBI or no recent history of mTBI (control), had no significant cognitive impairment and had no illness that could explain balance deficits. Sensory weight scores were measured using CSMI tests (Peterka 2002). Briefly, a CSMI test elicits anterior-posterior sway through pseudorandom surface and/or visual display rotations allowing measurements of sensory weights that indicate the relative contributions of proprioceptive, vestibular or visual systems to balance (Peterka, 2002). Four sensory conditions were evaluated: Condition 1 (C1) – reliance on the vestibular system; Condition 2 (C2) – reliance on combined vestibular and visual systems; Condition 3 (C3) – reliance on combined proprioceptive and vestibular systems; and Condition (C4) – reliance on vestibular system with conflicting visual and proprioceptive information. Whilst this abstract only reports the sensory weighting scores, the CSMI provides additional functionally meaningful parameters (e.g., system time delay, sensory-to-motor transformation properties), which are evaluated in the larger study. Following baseline testing, patients were enrolled into a rehabilitation program (2x/week for 6 weeks) focused on maintaining balance under changing sensory conditions with increasing levels of difficulty (Fino, et al., 2017). Follow-up testing was conducted at the conclusion of the intervention for people with mTBI and six weeks after baseline testing in controls, to establish stability of CSMI measures.

Results: Changes in sensory weights were assessed using Cohen's *d* effect sizes and the values reported are sensory weight measures ranging between 0 and 1. Increased weight scores were exhibited by the rehabilitation group (Rehab) in each of the four conditions: C1 ($Rehab_{pre}$=0.43±0.03, $Rehab_{post}$=0.49±0.09, *d*=0.86); C2 ($Rehab_{pre}$=0.61±0.05, $Rehab_{post}$=0.69±0.02, *d*=1.87); C3 ($Rehab_{pre}$=0.87±0.08, $Rehab_{post}$=0.89±0.03, *d*=0.43); and C4

(Rehab$_{pre}$=0.36±0.07, Rehab$_{post}$=0.42±0.11, *d*=0.69). No differences were indicated for the controls in follow up testing for conditions C1 (Con$_{pre}$=0.49±0.08, Con$_{post}$=0.50±0.11, *d*=0.08) or C2 (Con$_{pre}$=0.71±0.06 Con$_{post}$=0.72±0.07, *d*=0.09), however, small effects were noted in the control group for C3 (Con$_{pre}$=0.91±0.05, Con$_{post}$=0.92±0.01, *d*=-0.30) and C4 (Con$_{pre}$=0.47±0.04, Con$_{post}$=0.49±0.07, *d*=0.42).
Conclusion: Increased weight scores across each of the conditions in the rehabilitation group suggest the ability to change sensory weights in mTBI subjects, with the vestibular and combined weights (vestibular + vision/ proprioception) moving toward values consistent with those of controls following the intervention.

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Slower turning velocity and increased coordination variability are associated with self-reported symptoms in adults with mTBI

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Background: Abnormal balance and gait is common among individuals following mild traumatic brain injury (mTBI), yet measures of standing balance and straight gait have not been associated with self-reported symptoms. In daily activity and operational environments, complex movements involving change of direction are common and require rapid, coordinated reorientation of the head and trunk towards the new direction of travel. However, turning gait has not been well explored in populations with mTBI. Individuals with mTBI may limit their reorientation velocities based on their symptoms as rapid head movements can exacerbate symptoms. We hypothesized that individuals with mTBI would reduce their reorientation velocity and increase the variability of head-to-trunk coordination compared to controls, and that the reduction in velocity and increased variability would be associated with their self-reported symptom score.

Methods: Thirty-five young adults (10 mTBI, 25 controls) provided informed consent. All mTBI participants had self-reported complaints of imbalance and a diagnosed mTBI for >3 months. Each participant completed the Neurobehavioral Symptom Inventory (NSI) before walking 12 self-paced continuous laps around a marked course containing two 45° turns, four 90° turns, and two 135° turns. The first and last laps were excluded from analysis. Walking speed was determined from the average lap completion time. Inertial sensors affixed over the forehead and lumbar region collected angular velocities of the head and trunk, respectively. Angular velocities were low-pass filtered at 1.5 Hz. For each turn, the magnitude and time of peak axial angular velocity was extracted. Head-to-trunk coordination was defined using lag time, calculated as the difference in time between peak velocities of the head and trunk for each turn. For each participant, peak angular velocities were averaged across turns of the same angle. Lag times were averaged across all turns. Lag time variability was determined from the standard deviation of lag times. Linear mixed models compared the average peak angular velocities between groups after adjusting for covariates of turning angle and speed. Independent sample t-tests compared lag time and lag time variability between groups. Pearson correlation coefficients compared the relationship between each outcome and NSI symptom scores in the mTBI group.

Results: After adjusting for walking speed and turning angle, participants with mTBI had significantly slower peak angular velocities of the head (p=0.01, β=-0.24, SE=0.10) and trunk (p<0.01 β=-0.29, SE=0.09) compared to the control group. Average lag time did not differ between groups, but lag time variability was significantly higher in mTBI participants (p<0.01, g=0.58). Within the mTBI group, NSI total symptom scores were associated with slower average peak angular velocities of the head and trunk during 90° turns. Lag time variability was strongly associated with NSI symptom scores (r=0.87, p<0.01).

Conclusions: Individuals with mTBI adopted slower turning velocities and exhibited more variable head-to-trunk coordination timings compared to controls. The association of turning velocity and head-to-trunk coordination variability to self-reported symptoms suggests individuals with mTBI may change reorientation patterns to minimize the exacerbation of symptoms. These results provide knowledge of how self-reported symptoms influence daily locomotor function in adults with mTBI.

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Research Report

TITLE: Rehabilitation and sensory reweighting in patients with chronic mTBI

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Purpose/Hypothesis: Abnormal use of vestibular and visual systems may be linked to postural instability in patients with mild traumatic brain injury (mTBI)[1-3]. The aim of this study is to assess the effects of rehabilitation on sensory contributions to balance in chronic mTBI patients. Here we present preliminary data from a novel test of central sensorimotor integration (CSMI)[4].

Number of Subjects: 13

Materials/Methods: 6 patients (age=36±8) with chronic mTBI and 7 controls (age=25±6) with no recent history of mTBI were recruited. Patients with mTBI were tested at baseline and then again after a 6 week (2x/week)[5] balance rehabilitation program. The dizziness handicap inventory (DHI) was used to assess changes in symptoms. Controls were tested 6 weeks apart to assess CSMI test-retest reliability.

The CSMI test uses pseudorandom rotations of the surface and/or visual display to elicit anterior-posterior sway. Here, we report on 2 of the relevant visual and vestibular conditions: C1) 2° surface rotations - eyes closed, and C2) 2° surface rotations - eyes open. The CSMI analysis yields measures of sensory weights (W, the relative contribution of vestibular information to balance in C1 and the vestibular + visual contribution to balance in C2), and measures of sensorimotor stiffness (Kp) and damping (Kd) parameters, indicating the corrective ankle torque generated in proportion to the body sway angle and sway angular velocity, respectively. Consistency of the CSMI test was assessed using Intraclass Correlation Coefficients (ICCs). Changes in the mTBI group were assessed using effect sizes. Reported values for W range between 0 and 1, while Kp and Kd were normalized by each person's height and weight.

Results: Good to excellent consistency was found for each measure; C1: W, *ICC* =.92, CI[.42,.99]; Kp, *ICC*=.88, CI[.12,.98]; Kd, *ICC*=.97, CI[.80,.99]; C2: W, *ICC*=.80, CI[.14,.97]; Kp, *ICC*=.93, CI[.59,.99]; Kd *ICC*=.93, CI[.60,.99]. Following rehabilitation, W increased in both conditions toward control values (C1: pre=.41±.05, post=.47±.08, *d*=.92; C2: pre=.53±.04, post=.60±.05, *d*=1.64). Kp increased in C1 (pre=1.58±.23, post=1.66±.25, *d*=.34) but decreased in C2 (pre=1.94±.41, post=1.77±.28, *d*=-.52), while for Kd, effects indicated an increase in Kd for C1 and C2, respectively. (C1: pre=.48±.06, post=.55±.03, *d*=1.50; C2: pre=.50±.06,

post=.52±.08, *d*=.31). DHI improved in 5/6 patients, with an overall decrease in symptoms (pre=43±17, post=36±23, *d*=-.36).
Conclusions: CSMI test-retest results were highly consistent suggesting it may be an effective way to identify specific abnormalities and track changes in balance control. Increased W in the mTBI group toward control values suggests that rehabilitation changed reliance on sensory systems for balance. Differences in Kp and Kd following rehabilitation indicate adaptation in motor response to the stimuli. Decreased DHI suggests improvement in dizziness symptoms after rehabilitation.
Clinical Relevance: Understanding how sensory and sensorimotor contributions to balance change with rehabilitation may help drive evidence-based programs.
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Sensory weighting and rehabilitation in adults suffering chronic mTBI

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This abstract presents preliminary findings assessing the effects of rehabilitation on sensory weighting in patients with chronic balance impairment following mTBI. Nine patients (age=39.4±9.9) with chronic mTBI and seven controls (age=25.9±6.1) with no recent history of mTBI were recruited. Patients with mTBI were tested at baseline and then again after a 6 week (2x/week) balance rehabilitation program. The dizziness handicap inventory (DHI) was used to assess changes in symptoms. A novel test of central sensorimotor integration (CSMI) was used to collect measures of sensory weight (W, the relative contribution of vestibular and visual information to balance, range 0-100%), sensorimotor stiffness (Kp) and damping (Kd) parameters. Kp and Kd indicate the corrective ankle torque generated in proportion to the body sway angle and sway angular velocity, respectively. Here, we report on one condition that targets the visual and vestibular system. Between-group differences at baseline and within-group changes in the mTBI group following rehabilitation were assessed using Cohen's d effect sizes. Baseline results indicated lower W (control=71±6%, mTBI=63±6%, *d*=-1.43), Kp (control=1.73±0.36, mTBI=1.57±0.22, *d*=-0.57), and Kd (con=0.57±0.10, mTBI=0.47±0.06, *d*=-1.17) in the mTBI group compared with controls. Following rehabilitation, all measures increased toward control values (W: pre=63±6%, post=69±4%, *d*=1.20; Kp: pre=1.57±0.22, post=1.61±0.10, *d*=0.26; Kd: pre=0.47±0.06, post=0.53±0.03, *d*=1.22). DHI improved in 6/9 patients, with an overall decrease in symptoms (pre=45±15, post=39±21, *d*=-0.34). Results suggest people with chronic mTBI weight sensory information differently and exhibit a different motor response to stimuli. Increased W, Kp and Kd following rehabilitation suggests the potential for rehabilitation to change how people rely on sensory information and their motor response. Paired with the decrease in DHI, initial evidence suggests rehabilitation may improve physical function and symptoms.

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Title: Abnormal turning and its association with self-reported symptoms in chronic mTBI

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Mentor: Laurie King
Co-Authors: Lucy Parrington, Merissa Walls, Emily Sippel, Timothy Hullar, James Chesnutt, Laurie King

Abstract: Turning is common in daily activity and requires rapid, coordinated reorientation of the head and trunk, and pelvis towards the new direction of travel. Yet, turning gait has not been well explored in populations with mild traumatic brain injury (mTBI) who may alter their turning behavior according to self-perceived symptoms or motor dysfunction. The purpose of this study was to examine turning velocities and coordination in adults with chronic mTBI (>3 months post-injury and still reporting balance complaints) during a task simulating everyday ambulation. We hypothesized that individuals with chronic mTBI would reduce their angular velocity when turning and increase the variability of head-pelvis coordination compared to controls, and that the reduction in velocity and increased variability would be associated with their self-reported symptom score. Forty-two adults (14 chronic mTBI, 28 controls) completed the Neurobehavioral Symptom Inventory before walking 12 laps around a marked course containing two 45° turns, four 90° turns, and two 135° turns. Inertial sensors collected angular velocities of the head and pelvis. After adjusting for covariates, participants with chronic mTBI had significantly slower lap times and peak angular velocities of the pelvis ($p<0.01$) compared to the control group. The peak velocity timing (PVT) between peak velocities of the head and pelvis, and the variability of that timing was significantly greater in chronic mTBI participants ($p<0.01$). Within the chronic mTBI group, somatosensory symptoms were associated with slower angular velocities of the head and pelvis ($p=0.03$) and increased PVT variability ($p<0.01$). The results suggest individuals with chronic mTBI with worse somatic symptoms have impaired head stabilization during turning in situations similar to everyday life. These results encourage future research on turning gait to examine the causal relationship between symptoms and daily locomotor function in adults with chronic mTBI.